

AMENDMENTS TO THE SPECIFICATION

Please make the following amendments to the specification.

Please replace paragraph 0029 with the following replacement paragraph:

Reference is made to the sequence listing attached hereto, which consists of the following files: SEQ_LIST_EFS19_amended_Feb_2007_001.txt (23,553 kb), SEQ_LIST_EFS19_amended_Feb_2007_002.txt (23,553 kb), SEQ_LIST_EFS19_amended_Feb_2007_001.txt (16,397 kb) the file Patent19_Virus_patentIn_0508_1.txt (63,519 KB), which were was created February 20, 2007 on May 15, 2008, and which altogether are is a sequence listing in accordance with 37 C.F.R. §§ 1.821-1.825, the contents of which are incorporated by reference herein.

Please replace paragraph 0050 with the following replacement paragraph:

A Hairpin ~~Structure~~Structure is defined as an oligonucleotide having a nucleotide sequence that is 50-140 nucleotides in length, the first half of which nucleotide sequence is at least partially complementary to the second part thereof, thereby causing the nucleic acid to fold onto itself, forming a secondary hairpin structure.

Please replace paragraph 0073 with the following replacement paragraph:

Fig. 13A and Fig. 13B are a picture and a summary table of laboratory results validating the expression of novel human oligonucleotides detected by a bioinformatic oligonucleotide detection engine constructed and operative in accordance with a preferred embodiment of the present invention, thereby validating the efficacy of the oligonucleotide detection engine of the present invention. The sequences in Fig. 13B have SEQ ID NOS: 399754-399804;

Please replace paragraph 0075 with the following replacement paragraph:

Fig. 14B is a schematic representation of secondary folding of hairpins of the operon-like cluster of Fig. 14A. The hairpins are associated with the following SEQ ID NOS: N2 (SEQ ID NO: 399805); N3 (SEQ ID NO: 399806); MIR23 (SEQ ID NO: 399807); GAM22 (SEQ ID NO: 399808); GAM116 (SEQ ID NO: 399809); N116 (SEQ ID NO: 399810); N4 (SEQ ID NO: 399811); N0 (SEQ ID NO: 399812); N6 (SEQ ID NO: 399813); MIR24 (SEQ ID NO: 399814); N7 (SEQ ID NO: 399815);

Please replace paragraph 0077 with the following replacement paragraph:

Fig. 15A is an annotated sequence of EST72223 (SEQ ID NO: 399816) comprising known human miRNA oligonucleotide MIR98 (SEQ ID NO: 399817) and novel human oligonucleotide GAM25 PRECURSOR (SEQ ID NO: 399819) detected by the oligonucleotide detection system of the present invention. The sequences in Fig. 15A have the following SEQ ID NOs: EST (SEQ ID NO: 399816); Pal 98 (SEQ ID NO: 399817); MIR 98 (SEQ ID NO: 399818) Pal GAM 25 (SEQ ID NO: 399819); Pal GAM 25 (SEQ ID NO: 399820); and

Please replace paragraph 0079 with the following replacement paragraph:

Fig. 16 presents pictures of laboratory results demonstrating laboratory confirmation of 'dicing' of four novel bioinformatically detected HIV1 GAM PRECURSORSs (SEQ ID NOs: 399821-399825) into their corresponding mature GAM RNAs, herein designated VGAM2032-B (Fig. 16B), VGAM3249-A (Fig. 16C), GAM507-B (Fig. 16D) (SEQ ID NOs: 399826-399828) and VGAM1016-B (Fig. 16E) (SEQ ID NOs: 399829-399831);

Please replace paragraph 0178 with the following replacement paragraph:

UTR of GAM viral target genes were preferably extracted directly from annotation of UTR records. Alternatively, UTR of GAM viral target genes were preferably extracted by taking the sequences spanned from last coding position to the 3 end of the mRNA sequence annotation. Alternatively, UTR of GAM viral target genes were preferably extracted by taking 400 nucleotides downstream to the encoding region of the mRNA sequence. All of abovemention methods were applied on complete viral genomes data in GeneBank format from the NCBI RefSeq database, version 18-Jan-2004 (<ftp://ftp.ncbi.nih.gov/refseq/release/viral>).

Please replace paragraphs 0211-0214 with the following replacement paragraphs:

[0211] Fractionation was done by loading up to 500g per YM100 Amicon Microcon column (Millipore) followed by a 500g centrifugation for 40 minutes at 4C. Flow through "YM100"RNA consisting of about of the total RNA was used for library preparation or fractionated further by loading onto a YM30 Amicon Microcon column (Millipore) followed by a 13,500g centrifugation for 25 minutes at 4C. Flowthrough "YM30" was used for library preparation as is and consists of less than 0.5% of total RNA. For the both the "ligation" and the "One-tailed" libraries, RNA was dephosphorilated and ligated to an RNA (lowercase)-DNA (UPPERCASE) hybrid 5-phosphorilated, 3 idT blocked 3-adapter (5-P-uuuAACCGCATCCTTCTC-idT-3 (SEQ ID NO: 399739) Dharmacon # P-002045-01-05) (as elaborated in Elbashir et al., Genes Dev. 15:188-200 (2001)) resulting in ligation only of RNase III type cleavage

products. 3-Ligated RNA was excised and purified from a half 6%, half 13% polyacrylamide gel to remove excess adapter with a Nanosep 0.2M centrifugal device (Pall) according to instructions, and precipitated with glycogen and 3 volumes of Ethanol. Pellet was resuspended in a minimal volume of water.

[0212] For the "ligation" library a DNA (UPPERCASE)-RNA (lowercase) hybrid 5-adapter (5-TACTAATACGACTCACTaaa-3 Dharmacon # P-002046-01-05) (SEQ ID NO: 399740) was ligated to the 3-adapted RNA, reverse transcribed with "EcoRI-RT": (5-GACTAGCTGGAATTCAAGGATGCGGTTAAA-3), (SEQ ID NO: 399741) PCR amplified with two external primers essentially as in Elbashir et al 2001 except that primers were "EcoRI-RT" and "PstI Fwd"(5- CAGCCAACGCTGCAGATACGACTCACTAAA-3) (SEQ ID NO: 399742). This PCR product was used as a template for a second round of PCR with one hemispecific and one external primer or with two hemispecific primers.

[0213] For the "One tailed" library the 3-Adapted RNA was annealed to 20pmol primer "EcoRI RT" by heating to 70C and cooling 0.1C/sec to 30C and then reverse transcribed with Superscript II RT (According to instructions, Invitrogen) in a 20l volume for 10 alternating 5 minute cycles of 37C and 45C. Subsequently, RNA was digested with 11 2M NaOH, 2mM EDTA at 65C for 10 minutes. cDNA was loaded on a polyacrylamide gel, excised and gel-purified from excess primer as above (invisible, judged by primer run alongside) and resuspended in 13l of water. Purified cDNA was then oligo-dC tailed with 400U of recombinant terminal transferase (Roche molecular biochemicals), 11 100M dCTP, 11 15mM CoCl₂, and 4l reaction buffer, to a final volume of 20l for 15 minutes at 37C. Reaction was stopped with 2l 0.2M EDTA and 15l 3M NaOAc pH 5.2. Volume was adjusted to 150l with water, Phenol: Bromochloropropane 10:1 extracted and subsequently precipitated with glycogen and 3 volumes of Ethanol. C-tailed cDNA was used as a template for PCR with the external primers "T3-PstBsg(G/I)18"(5-AATTAAACCCTCACTAAAGGCTGCAGGTGCAGGIGGGIIGGGIIGG GIIGN-3 (SEQ ID NO: 399743) where I stands for Inosine and N for any of the 4 possible deoxynucleotides), and with "EcoRI Nested"(5-GGAATTCAAGGATGCGGTTA-3) (SEQ ID NO: 399744). This PCR product was used as a template for a second round of PCR with one hemispecific and one external primer or with two hemispecific primers.

[0214] Hemispecific primers were constructed for each predicted GAM RNA oligonucleotide by an in-house program designed to choose about half of the 5 or 3 sequence of the GAM RNA corresponding to a TM of about 30-34C constrained by an optimized 3 clamp, appended to the cloning adapter sequence (for "One-tailed" libraries 5-GGNNGGGNNG on the 5 end (SEQ ID NO: 399745) of the GAM RNA , or TTTAACCGCATC-3 (SEQ ID NO: 399746) on the 3 end of the GAM RNA. For "Ligation" libraries the same 3 adapter and 5-CGACTCACTAAA on the 5 end) (SEQ ID NO: 399747). Consequently, a fully complementary primer of a TM higher than 60C was created

covering only one half of the GAM RNA sequence permitting the unbiased elucidation by sequencing of the other half.

Please replace paragraph 0235 with the following replacement paragraph:

Transcript products were 705nt (EST72223), 102nt (MIR98 precursor), 125nt (GAM25 precursor) long. EST72223 was PCR amplified with T7-EST 72223 forward primer: 5-
TAATACGACTCACTATAAGGCCATTATTAGAGGATTCTGCT-3
(SEQ ID NO: 399748). and T3-EST72223 reverse primer:"-
AATTAACCCTCACTAAAGGTTTTTTCCTGAGACAGAGT- 3
(SEQ ID NO: 399749). MIR98 was PCR amplified using EST72223 as a template with T7MIR98 forward primer: 5-
TAATACGACTCACTATAAGGTGAGGTAGTAAGTTGTATTGTT
(SEQ ID NO: 399750). 3and T3MIR98 reverse primer: 5-
AATTAACCCTCACTAAAGGGAAAGTAGTAAGTTGTATAGTT- 3
(SEQ ID NO: 399751). GAM25 was PCR amplified using EST72223 as a template with GAM25 forward primer: 5-
GAGGCAGGAGAATTGCTTGA-3 (SEQ ID NO: 399752) and T3-EST72223 reverse primer:5-
AATTAACCCTCACTAAAGGCCTGAGACAGAGTCTTGCTC-3
(SEQ ID NO: 399753).